

Third Amended Sequence Listing

<110> Cheng, Winston T.K.

Chen, Chuan-Mu

Lin, Shwu-Wha

Wang, Chih-Hong

Lin, Chih-Jen

Wu, Shinn-Chih



<120> Method for producing biologically active human factor VIII  
in the milk of transgenic animals driven by mammary-specific  
expression cassettes

<130> 683884-2US

<140> US 10/820,777

<141> 2004-04-09

<160> 15

<170> PatentIn version 3.2

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<213> Artificial

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<223> Synthetic

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aac 63

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<212> DNA

<213> Homo sapiens

<400> 11

cattctattc atttcagtg gg aca

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<210> 12

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<212> DNA

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<211> 19

<212> PRT

<213> Bovine

<400> 13

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Ala Thr Glu Ala

<210> 14

<211> 15

<212> PRT

<213> Bovine

<400> 14

Met Lys Leu Leu Ile Leu Thr Cys Leu Val Ala Val Ala Ala Arg

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<213> Artificial

<220>

<223> Bovine-Homo sapiens fusion protein

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Met Lys Leu Leu Ile Leu Thr Cys Leu Val Ala Val Ala Ala Arg Leu

5

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15

Thr Ala Thr Arg Arg Tyr Tyr Leu Gly Ala Val Glu Leu Ser  
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 Trp Asp Tyr Met Gln Ser Asp Leu Gly Glu Leu Pro Val Asp Ala Arg  
 35 40 45  
 Phe Pro Pro Arg Val Pro Lys Ser Phe Pro Phe Asn Thr Ser Val Val  
 50 55 60  
 Tyr Lys Lys Thr Leu Phe Val Glu Phe Thr Asp His Leu Phe Asn Ile  
 65 70 75  
 Ala Lys Pro Arg Pro Pro Trp Met Gly Leu Leu Gly Pro Thr Ile Gln  
 80 85 90  
 Ala Glu Val Tyr Asp Thr Val Val Ile Thr Leu Lys Asn Met Ala Ser  
 95 100 105 110  
 His Pro Val Ser Leu His Ala Val Gly Val Ser Tyr Trp Lys Ala Ser  
 115 120 125  
 Glu Gly Ala Glu Tyr Asp Asp Gln Thr Ser Gln Arg Glu Lys Glu Asp  
 130 135 140  
 Asp Lys Val Phe Pro Gly Gly Ser His Thr Tyr Val Trp Gln Val Leu  
 145 150 155  
 Lys Glu Asn Gly Pro Met Ala Ser Asp Pro Leu Cys Leu Thr Tyr Ser  
 160 165 170  
 Tyr Leu Ser His Val Asp Leu Val Lys Asp Leu Asn Ser Gly Leu Ile  
 175 180 185 190  
 Gly Ala Leu Leu Val Cys Arg Glu Gly Ser Leu Ala Lys Glu Lys Thr  
 195 200 205  
 Gln Thr Leu His Lys Phe Ile Leu Leu Phe Ala Val Phe Asp Glu Gly  
 210 215 220  
 Lys Ser Trp His Ser Glu Thr Lys Asn Ser Leu Met Gln Asp Arg Asp  
 225 230 235

Ala Ala Ser Ala Arg Ala Trp Pro Lys Met His Thr Val Asn Gly Tyr  
240 245 250

Val Asn Arg Ser Leu Pro Gly Leu Ile Gly Cys His Arg Lys Ser Val  
255 260 265 270

Tyr Trp His Val Ile Gly Met Gly Thr Thr Pro Glu Val His Ser Ile  
275 280 285

Phe Leu Glu Gly His Thr Phe Leu Val Arg Asn His Arg Gln Ala Ser  
290 295 300

Leu Glu Ile Ser Pro Ile Thr Phe Leu Thr Ala Gln Thr Leu Leu Met  
305 310 315

Asp Leu Gly Gln Phe Leu Leu Phe Cys His Ile Ser Ser His Gln His  
320 325 330

Asp Gly Met Glu Ala Tyr Val Lys Val Asp Ser Cys Pro Glu Glu Pro  
335 340 345 350

Gln Leu Arg Met Lys Asn Asn Glu Glu Ala Glu Asp Tyr Asp Asp Asp  
355 360 365

Leu Thr Asp Ser Glu Met Asp Val Val Arg Phe Asp Asp Asn Ser  
370 375 380

Pro Ser Phe Ile Gln Ile Arg Ser Val Ala Lys Lys His Pro Lys Thr  
385 390 395

Trp Val His Tyr Ile Ala Ala Glu Glu Asp Trp Asp Tyr Ala Pro  
400 405 410

Leu Val Leu Ala Pro Asp Asp Arg Ser Tyr Lys Ser Gln Tyr Leu Asn  
415 420 425 430

Asn Gly Pro Gln Arg Ile Gly Arg Lys Tyr Lys Lys Val Arg Phe Met  
435 440 445

Ala Tyr Thr Asp Glu Thr Phe Lys Thr Arg Glu Ala Ile Gln His Glu  
450 455 460

Ser Gly Ile Leu Gly Pro Leu Leu Tyr Gly Glu Val Gly Asp Thr Leu  
465 470 475

Leu Ile Ile Phe Lys Asn Gln Ala Ser Arg Pro Tyr Asn Ile Tyr Pro  
480 485 490

His Gly Ile Thr Asp Val Arg Pro Leu Tyr Ser Arg Arg Leu Pro Lys  
495 500 505 510

Gly Val Lys His Leu Lys Asp Phe Pro Ile Leu Pro Gly Glu Ile Phe  
515 520 525

Lys Tyr Lys Trp Thr Val Thr Val Glu Asp Gly Pro Thr Lys Ser Asp  
530 535 540

Pro Arg Cys Leu Thr Arg Tyr Tyr Ser Ser Phe Val Asn Met Glu Arg  
545 550 555

Asp Leu Ala Ser Gly Leu Ile Gly Pro Leu Leu Ile Cys Tyr Lys Glu  
560 565 570

Ser Val Asp Gln Arg Gly Asn Gln Ile Met Ser Asp Lys Arg Asn Val  
575 580 585 590

Ile Leu Phe Ser Val Phe Asp Glu Asn Arg Ser Trp Tyr Leu Thr Glu  
595 600 605

Asn Ile Gln Arg Phe Leu Pro Asn Pro Ala Gly Val Gln Leu Glu Asp  
610 615 620

Pro Glu Phe Gln Ala Ser Asn Ile Met His Ser Ile Asn Gly Tyr Val  
625 630 635

Phe Asp Ser Leu Gln Leu Ser Val Cys Leu His Glu Val Ala Tyr Trp  
640 645 650

Tyr Ile Leu Ser Ile Gly Ala Gln Thr Asp Phe Leu Ser Val Phe Phe  
655 660 665 670

Ser Gly Tyr Thr Phe Lys His Lys Met Val Tyr Glu Asp Thr Leu Thr  
675 680 685

Leu Phe Pro Phe Ser Gly Glu Thr Val Phe Met Ser Met Glu Asn Pro  
690 695 700  
Gly Leu Trp Ile Leu Gly Cys His Asn Ser Asp Phe Arg Asn Arg Gly  
705 710 715  
Met Thr Ala Leu Leu Lys Val Ser Ser Cys Asp Lys Asn Thr Gly Asp  
720 725 730  
Tyr Tyr Glu Asp Ser Tyr Glu Asp Ile Ser Ala Tyr Leu Leu Ser Lys  
735 740 745 750  
Asn Asn Ala Ile Glu Pro Arg Ser Leu Lys Arg His Gln Arg Glu Ile  
755 760 765  
Thr Arg Thr Thr Leu Gln Ser Asp Gln Glu Glu Ile Asp Tyr Asp Asp  
770 775 780  
Thr Ile Ser Val Glu Met Lys Lys Glu Asp Phe Asp Ile Tyr Asp Glu  
785 790 795  
Asp Glu Asn Gln Ser Pro Arg Ser Phe Gln Lys Lys Thr Arg His Tyr  
800 805 810  
Phe Ile Ala Ala Val Glu Arg Leu Trp Asp Tyr Gly Met Ser Ser Ser  
815 820 825 830  
Pro His Val Leu Arg Asn Arg Ala Gln Ser Gly Ser Val Pro Gln Phe  
835 840 845  
Lys Lys Val Val Phe Gln Glu Phe Thr Asp Gly Ser Phe Thr Gln Pro  
850 855 860  
Leu Tyr Arg Gly Glu Leu Asn Glu His Leu Gly Leu Leu Gly Pro Tyr  
865 870 875  
Ile Arg Ala Glu Val Glu Asp Asn Ile Met Val Thr Phe Arg Asn Gln  
880 885 890  
Ala Ser Arg Pro Tyr Ser Phe Tyr Ser Ser Leu Ile Ser Tyr Glu Glu  
895 900 905 910

Asp Gln Arg Gln Gly Ala Glu Pro Arg Lys Asn Phe Val Lys Pro Asn  
915 920 925

Glu Thr Lys Thr Tyr Phe Trp Lys Val Gln His His Met Ala Pro Thr  
930 935 940

Lys Asp Glu Phe Asp Cys Lys Ala Trp Ala Tyr Phe Ser Asp Val Asp  
945 950 955

Leu Glu Lys Asp Val His Ser Gly Leu Ile Gly Pro Leu Leu Val Cys  
960 965 970

His Thr Asn Thr Leu Asn Pro Ala His Gly Arg Gln Val Thr Val Gln  
975 980 985 990

Glu Phe Ala Leu Phe Phe Thr Ile Phe Asp Glu Thr Lys Ser Trp Tyr  
995 1000 1005

Phe Thr Glu Asn Met Glu Arg Asn Cys Arg Ala Pro Cys Asn Ile Gln  
1010 1015 1020

Met Glu Asp Pro Thr Phe Lys Glu Asn Tyr Arg Phe His Ala Ile Asn  
1025 1030 1035

Gly Tyr Ile Met Asp Thr Leu Pro Gly Leu Val Met Ala Gln Asp Gln  
1040 1045 1050

Arg Ile Arg Trp Tyr Leu Leu Ser Met Gly Ser Asn Glu Asn Ile His  
1055 1060 1065 1070

Ser Ile His Phe Ser Gly His Val Phe Thr Val Arg Lys Lys Glu Glu  
1075 1080 1085

Tyr Lys Met Ala Leu Tyr Asn Leu Tyr Pro Gly Val Phe Glu Thr Val  
1090 1095 1100

Glu Met Leu Pro Ser Lys Ala Gly Ile Trp Arg Val Glu Cys Leu Ile  
1105 1110 1115

Gly Glu His Leu His Ala Gly Met Ser Thr Leu Phe Leu Val Tyr Ser  
1120 1125 1130

Asn Lys Cys Gln Thr Pro Leu Gly Met Ala Ser Gly His Ile Arg Asp  
1135                    1140                    1145                    1150

Phe Gln Ile Thr Ala Ser Gly Gln Tyr Gly Gln Trp Ala Pro Lys Leu  
1155                    1160                    1165

Ala Arg Leu His Tyr Ser Gly Ser Ile Asn Ala Trp Ser Thr Lys Glu  
1170                    1175                    1180

Pro Phe Ser Trp Ile Lys Val Asp Leu Leu Ala Pro Met Ile Ile His  
1185                    1190                    1195

Gly Ile Lys Thr Gln Gly Ala Arg Gln Lys Phe Ser Ser Leu Tyr Ile  
1200                    1205                    1210

Ser Gln Phe Ile Ile Met Tyr Ser Leu Asp Gly Lys Lys Trp Gln Thr  
1215                    1220                    1225                    1230

Tyr Arg Gly Asn Ser Thr Gly Thr Leu Met Val Phe Phe Gly Asn Val  
1235                    1240                    1245

Asp Ser Ser Gly Ile Lys His Asn Ile Phe Asn Pro Pro Ile Ile Ala  
1250                    1255                    1260

Arg Tyr Ile Arg Leu His Pro Thr His Tyr Ser Ile Arg Ser Thr Leu  
1265                    1270                    1275

Arg Met Glu Leu Met Gly Cys Asp Leu Asn Ser Cys Ser Met Pro Leu  
1280                    1285                    1290

Gly Met Glu Ser Lys Ala Ile Ser Asp Ala Gln Ile Thr Ala Ser Ser  
1295                    1300                    1305                    1310

Tyr Phe Thr Asn Met Phe Ala Thr Trp Ser Pro Ser Lys Ala Arg Leu  
1315                    1320                    1325

His Leu Gln Gly Arg Ser Asn Ala Trp Arg Pro Gln Val Asn Asn Pro  
1330                    1335                    1340

Lys Glu Trp Leu Gln Val Asp Phe Gln Lys Thr Met Lys Val Thr Gly  
1345                    1350                    1355

Val Thr Thr Gln Gly Val Lys Ser Leu Leu Thr Ser Met Tyr Val Lys  
1360 1365 1370

Glu Phe Leu Ile Ser Ser Ser Gln Asp Gly His Gln Trp Thr Leu Phe  
1375 1380 1385 1390

Phe Gln Asn Gly Lys Val Lys Val Phe Gln Gly Asn Gln Asp Ser Phe  
1395 1400 1405

Thr Pro Val Val Asn Ser Leu Asp Pro Pro Leu Leu Thr Arg Tyr Leu  
1410 1415 1420

Arg Ile His Pro Gln Ser Trp Val His Gln Ile Ala Leu Arg Met Glu  
1425 1430 1435

Val Leu Gly Cys Glu Ala Gln Asp Leu Tyr  
1440 1445